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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/997,424	11/28/2001	Kimberly A. Gillis	102729-16	6432
21125	7590	02/25/2005	EXAMINER	
NUTTER MCCLENNEN & FISH LLP WORLD TRADE CENTER WEST 155 SEAPORT BOULEVARD BOSTON, MA 02210-2604			DAVIS, MINH TAM B	
			ART UNIT	PAPER NUMBER
			1642	

DATE MAILED: 02/25/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

Application No.

09/997,424

Applicant(s)

GILLIS ET AL.

Examiner

MINH-TAM DAVIS

Art Unit

1642

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 13 December 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 35 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 35 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

### **DETAILED ACTION**

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1-34 have been cancelled and replaced with new claim 35. Claim 35 is no longer a linking claim because no dependent claims directed to distinct inventions are present and linked by Claim 35. Should claims be filed which results in re-instatement of Claim 35 as a linking claim, the Examiner may follow the practice set forth in MPEP 809.

Accordingly, claim 35, SMARCD3 comprising SEQ ID NO:5, is examined in the instant application.

The following are the remaining rejections.

### **REJECTION UNDER 35 USC 112, SECOND PARAGRAPH, NEW REJECTION**

Claim 35 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01.

The omitted steps are: 1) Comparing the result of the test sample to that of the control sample, 2) Correlation between the results and the preamble.

### **REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, NEW MATTER, NEW REJECTION**

Claim 35 is rejected under 35 USC 112, first paragraph, as the specification does not contain a written description of the claimed invention.

1. The limitation of “diagnosing development” of prostate cancer claimed in Claim 35 has no clear support in the specification and the claims as originally filed.

A review of the specification discloses support for diagnosis of the presence or potential presence of prostate cancer in a subject (p.7, lines 13-14), or markers for risk of development of prostate cancer (p.10, lines 13-14). There is however no mention of “diagnosing development” of prostate cancer.

**The subject matter claimed in claims broadens the scope of the invention as originally disclosed in the specification.**

2. The limitation of “prognosis of progression” of prostate cancer claimed in Claim 35 has no clear support in the specification and the claims as originally filed.

A review of the specification discloses support for monitoring progression of prostate cancer in a subject (p.4, lines 5-6), and prognosis of prostate disorders (p.2, line 24), correlated with risk of development of prostate cancer (p.10, lines 14-15). There is however no mention of “prognosing development” of prostate cancer.

**The subject matter claimed in claims broadens the scope of the invention as originally disclosed in the specification.**

#### **REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, ENABLEMENT**

- A. Claim 35 is rejected under 35 USC 112, first paragraph, pertaining to lack of enablement for a method for detecting the presence of prostate cancer, comprising

detecting an a decrease in the expression of SMARCD3 in a sample of prostate cells, wherein SMARCD3 comprises SEQ ID NO:5.

(I) Applicant submits a Declaration by Dr. Steven Haney, stating that 1) the identified marker, SMARCD-3, was found to be significantly differentially expressed between diseased and normal tissues, 2) the cell line LNCaP is a well-established cell line model of human prostat cancer, and 3) those in the art, such as Horoszewicz et al, Thalmann et al, view LNCaP cells as in vitro model of prostate cancer, wherein LNCaP expresses prostatic acid phosphatase, androgen receptor, and PSA, which are hallmark of the prostatic phenotype.

Applicant asserts that well-characterized human cancer cell lines, such as LNCaP, are routinely used, and have proven to be highly predictive of in vivo results.

Applicant asserts that PSA was used as control, as was found to be increased as expected in prostate cancer cells.

The submission of the Declaration by Dr. Steven Haney, and the recitation of Horoszewicz et al, Thalmann et al is acknowledged and entered.

Applicant's arguments set forth in paper of 12/13/04 have been considered but are not deemed to be persuasive for the following reasons:

The specification discloses that a significant **difference** between the level of expression of the marker in the sample from the subject and normal level is an indication of prostate cancer (p. 3, first paragraph, p.7,last paragraph bridging p.8). The specification further discloses that the expression level of SMARCD3 decreases in LNCaP cells treated with androgen (p.77 of Example 1)

It is noted however that it is not clear from the specification, and in the Declaration whether there is a difference in mRNA levels of SMARCD3 (SEQ ID NO: 5) in primary prostate cancer tissue, as compared to normal control prostate tissue, nor is it clear that even if there is a difference, such difference is an increase or a decrease in mRNA levels of SMARCD3 (SEQ ID NO: 5) in primary prostate cancer tissue, as compared to normal control, in view that the only Example drawn to difference is from prostate cancer cell LNCaP studies, in which the expression of SMARCD3 decreases in androgen treated LNCaP cells, using ANOVA analysis, based on adaptation of the self-organizing map (SOM) algorithm (p.77).

**Expression of SMARCD3 being down-regulated by an androgen in a prostate cancer cell line is not in any way correlated with change in mRNA level of SMARCD3 in prostate cancer tissue as compared to normal control tissue, and is not an indication of the presence of prostate cancer.**

Although the specification discloses that genes with statistically significant difference between diseased and normal tissues were identified (p.7, last line bridging p.8), it appears that the example is based on detecting differential expression of SMARCD3 in prostate cell line LNCaP, in the presence and absence of androgen, and not in prostate cancer cells versus normal prostate cells. There is no indication that SMARCD3 is differentially expressed in any diseased tissues, including prostate cancer tissues versus normal control corresponding tissue, especially in view of 1) the unpredictability of level of expression of a gene in diseases or in cancer, 2) the lack of confirming data such that one can determine that SMARCD3 is differentially expressed

in prostate cancer tissues versus normal control corresponding tissue, and 3) further in view of the disclosure in Example 4 (p.79) , which states that RNA **can** (emphasis added) be isolated from normal prostate glands and prostate tumors with different Gleason grades, and examined using Affymetrix microarrays method of Example 1, for detection of SMARCD3 markers in solid tumors. In other words, it is clear that Applicant only contemplates detection of differential expression of SMARCD3 in differentially expressed in prostate cancer tissues versus normal control corresponding tissue, but has not in fact performed any analysis to determine whether statements drawn to SMARCD3 are in actuality based on fact.

It is not clear on what basis that the specification asserts that there is a differential expression of SMARCD3 mRNAs in primary prostate cancer tissue as compared to normal tissues, in view of that mutation or change in the level of expression of a gene is a chance event, and that not every gene in a cancer cell is affected in carcinogenesis, such as mutation or changes in expression as compared to normal control cells, as taught by Stanton, P et al, , lehle, C et al, and Abbaszadegan, M R, et al, all of record.

Thus without objective evidence, and in view that change in level of mRNA expression of a gene in a tumor as compared to normal corresponding cells is unpredictable, one cannot predict that the SMARCD3 polynucleotide of SEQ ID NO: 5 would be differentially expressed in primary prostate cancer tissues versus corresponding normal cells, based solely on its reduced expression in LNCaP cells treated with androgen.

In addition, a decrease in SMARCD3 mRNAs levels in LNCaP cells treated with androgen only indicates that SMARCD3 is sensitive to androgen treatment, and says nothing concerning diagnosis of prostate cancer, by detecting a decrease in the mRNAs level of the SMARCD3 of SEQ ID NO:5, because it is not clear what the levels of the mRNAs of the SMARCD3 of SEQ ID NO:5 are in the normal prostate tissue controls.

Concerning Applicant's arguments that well-characterized human cancer cell lines, such as LNCaP, are routinely used, and have proven to be highly predictive of in vivo results, the arguments are moot in view that **there is no correlation between a decrease in SMARCD3 mRNA levels in LNCaP cells treated with androgen and a decrease in SMARCD3 mRNA levels in primary prostate cancer cells as compared to normal prostate cancer cells as marker for diagnosis of prostate cancer**, in view of above reasons.

Moreover, even if Applicant shows that there is a decrease in SMARCD3 mRNA levels in prostate cancer cells LNCaP as compared to normal prostate cancer cells, one cannot predict that the level of expression of genes in cells in culture, including LNCaP, would be predictive of in vivo conditions, due to cell culture artifacts. Although LNCaP expresses prostatic acid phosphatase, androgen receptor, and PSA, as disclosed in the art recited in the Declaration by Dr. Steven Haney, one cannot predict that other genes, including the SMARCD3 of SEQ ID NO:5 would not be subjected to cell culture artifacts. Characteristics of cultured cell lines generally differ significantly from the characteristics of a primary tumor. Drexler et al (Leukemia and Lymphoma, 1993, 9:1-25) specifically teach, in the study of Hodgkin and Reed-Sternberg cancer cells in culture, that the



acquisition or loss of certain properties during adaptation to culture systems cannot be excluded and that only a few cell lines containing cells that resemble the *in-vivo* cancer cells have been established and even for the *bona fide* cancer cell lines it is difficult to prove that the immortalized cells originated from a specific cancer cell (see attached abstract). Further, Embleton et al (Immunol Ser, 1984, 23:181-207) specifically teaches that in procedures for the diagnosis of osteogenic sarcoma, caution must be used when interpreting results obtained with monoclonal antibodies that had been raised to cultured cell lines and specifically teach that cultured tumor cells may not be antigenically typical of the tumor cell population from which they were derived and it is well established that new artifactual antigens can occur as a result of culture (see attached abstract). Hsu (in Tissue Culture Methods and Applications, Kruse and Patterson, Eds, 1973, Academic Press, NY, see abstract, p.764) specifically teaches that it is well known that cell cultures *in vitro* frequently change their chromosomal constitutions (see abstract). The evidence presented clearly demonstrates that in cell culture systems, in general, and in cancer derived cell lines in particular, that artifactual chromosome constitutions and antigen expression are expected and must be taken into account when interpreting data received from cell line assays. Further, Freshney (Culture of Animal Cells, A Manual of Basic Technique, Alan R. Liss, Inc., 1983, New York, p4) teach that it is recognized in the art that there are many differences between cultured cells and their counterparts *in vivo*. These differences stem from the dissociation of cells from a three-dimensional geometry and their propagation on a two-dimensional substrate. Specific cell interactions characteristic of histology of the tissue are lost. The culture

environment lacks the input of the nervous and endocrine systems involved in homeostatic regulation *in vivo*. Without this control, cellular metabolism may be more constant *in vitro* but may not be truly representative of the tissue from which the cells were derived.

Further, PSA is not used as an internal control for detecting differential expression of SMARCD3 in diseased tissues, including prostate cancer tissues versus normal control corresponding tissue. The specification discloses that the level of PSA in the prostate cell line LNCaP is increased in the presence of DHT (figure 1B, and p.75, paragraph under results bridging p.76), while the expression level of SMARCD3 is decreased in the presence of the androgen DHT (p.77, last paragraph). The only common feature between PSA and SMARCD3 is that both are regulated by DHT in a prostate cancer cell line, which is not an indication that SMARCD3 is downregulated in prostate cancer tissues as compared to normal prostate tissues.

Thus, in the absence of objective evidence, expression of SMARCD3 being down-regulated by an androgen in a prostate cancer cell line, LNCaP, is not in any way correlated with change in mRNA level of SMARCD3 in prostate cancer tissue as compared to normal control tissue, and is not an indication of the presence of prostate cancer.

In view of the above, it would be undue experimentation for one of skill in the art to practice the claimed invention.

(II) In the Declaration, Dr. Steven Haney also argues that one would recognize the genes, which were found to be statistically significantly expressed, using a two-way

analysis of variance, in response to natural androgen in LNCaP, based on the Affymetrix Genechip screening of 68000 full length genes.

This is not found to be persuasive. In the absence of objective evidence, expression of SMARCD3 being down-regulated by an androgen in a prostate cancer cell line, LNCaP, is not in any way correlated with change in mRNA level of SMARCD3 in prostate cancer tissue as compared to normal control tissue, and is not an indication of the presence of prostate cancer, *supra*.

Further, The claimed method, as disclosed in the specification, is based on a flawed method, i.e. using Affymetrix for screening an underrepresentative number of genes. It is noted that from screening underrepresented libraries, a polynucleotide that is not expressed in one library or is expressed in another appears to be an artifact of the analytical system and cannot be extrapolated to a prediction of whether that the polynucleotide is over or underexpressed in the tissue "represented" by the library.

The claimed method is based on a screening an **underrepresentative** number of screened genes (6000 genes), even in view of the low figure of the number of protein-coding genes of 24, 5000 disclosed by J M Claverie, a reference submitted by Applicant. It is well known in the art that a complete cDNA library for use in screening a gene is one that contains at least one cDNA clone representing each mRNA in a cell, and that there are about 34,000 different types of mRNAs in a mammalian cells and about 500,000 mRNA molecules per cell, as taught in a commonly used text book by Ausubel et al, eds, of record. Ausubel et al further teach that if the number of molecules of the rarest mRNA in a cell is 8, the calculated number of clones that should be

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screened to achieve a 99% probability that a cDNA will exist in the library is 324,000.

Similarly, in another commonly used text book by Sambrook et al, eds, 1989 ( Molecular cloning, a Laboratory manual, 2<sup>nd</sup> ed, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, p.8.3-8.7, of record) Sambrook et al teach that a typical mammalian cell contains between 10,000 and 30,000 different mRNA sequences. Sambrook et al further teach that for low abundance mRNAs, i.e. 14 copies/cell, although the minimum clones required to obtain representation of mRNAs of this class is 37,000, but because of preferential cloning of certain sequences, a much larger number of recombinants must be obtained to increase the chances that any given clone will be represented in the library, i. e., about 170,000 clones (p.8.5 last paragraph, bridging p.8.7). Sambrook et al also teach that unfortunately, many mRNAs of interest are present at even lower level, i.e. 1 molecule/cell is not unusual. Thus based on the teaching in the art, it is clear that the cRNAs from a total of 6000 genes of the claimed invention would not be representative of all mRNAs present in a cell.

**B. Claim 35 is also rejected under 112, first paragraph because claim 35 encompasses a method for detecting the presence of prostate cancer, comprising detecting a decrease in the “protein levels” of the SMARCD3 protein encoded by the SMARCD3 polynucleotide of SEQ ID NO:5.**

Since one cannot predict that there is a decrease in the mRNA level of expression of the SMARCD3 polynucleotide of SEQ ID NO: 5 in prostate cancer, in view of lack of objective evidence and further in view of the teaching in the art, supra, one

cannot predict either that there is a decrease in the protein levels of the SMARCD3 protein encoded by SEQ ID NO:5.

Further, even if there is a decrease in the mRNA level of expression of SEQ ID NO:5 in prostate cancer, one cannot extrapolate the mRNA level of expression of SEQ ID NO:5 to the protein level of the corresponding encoded protein.

One cannot predict that protein levels are correlated with steady-state mRNA levels or alterations in mRNA levels. For instance, Brennan et al (Journal of Autoimmunity, 1989, vol. 2 suppl., pp. 177-186) teach that high levels of the mRNA for TNF alpha were produced in synovial cells, but that levels of the TNF alpha protein were undetectable. Further, Zimmer (Cell Motility and the Cytoskeleton, 1991, vol. 20, pp. 325-337) teaches that there is no correlation between the mRNA level of calcium-modulated protein S100 alpha and the protein level, indicating that S100 protein is post-transcriptionally regulated. Eriksson et al (Diabetologia, 1992, vol. 35, pp. 143-147) teach that no correlation was observed between the level of mRNA transcript from the insulin-responsive glucose transporter gene and the protein encoded thereby. Thus, cannot anticipate that the level of a specific mRNA expressed by a cell will be paralleled at the protein level due to complex homeostatic factors controlling translation and post-translational modification.

In view of the above, it would be undue experimentation for one of skill in the art to practice the claimed invention.

**C. Claim 35 is also rejected under 112, first paragraph because claim 35 encompasses a method for diagnosing development of or progression of**

**prostate cancer, comprising detecting a decrease in the expression of the SMARCD3 comprising SEQ ID NO:5.**

**Claim 35 encompasses a method for detecting development or progression of prostate cancer from preneoplastic conditions.**

In view of lack of objective evidence and further in view of the teaching in the art, supra, one cannot predict either that there is a decrease in the expression of the SMARCD3 comprising SEQ ID NO:5 during development of or progression of prostate cancer.

Further, even if there is an increase in the expression of SEQ ID NO: 5 in prostate cancer, there is no correlation between increase in the expression of SEQ ID NO:5 in development or progression of prostate cancer from preneoplastic conditions, because there is no indication that SEQ ID NO: 5 is responsible or involved in carcinogenesis of prostate cancer.

**D. Claim 35 is also rejected under 112, first paragraph because claim 35 encompasses a method for detecting risk of development of or progression of prostate cancer, comprising detecting an increase in the expression of the SMARCD3 comprising SEQ ID NO:5.**

Since one cannot predict that there is an increase in the expression of SEQ ID NO: 5 during development or progression of prostate cancer, in view of lack of objective evidence and further in view of the teaching in the art, supra, one cannot predict either that the expression of SEQ ID NO:5 in prostate cancer could be used for detecting risk of development of or progression of prostate cancer.

Further, even if there is an increase in the expression of SEQ ID NO:5 in prostate cancer, the specification provides neither guidance on nor exemplification of how to correlate the increase in the expression of SEQ ID NO:5 with the ability to use the increase in the expression of SEQ ID NO:5 for the assessment of risk of development of or progression of prostate cancer. Tockman et al (Cancer Res., 1992, 52:2711s-2718s) teach considerations necessary in bringing an cancer biomarker (intermediate end point marker) to successful clinical application. Although the reference is drawn to biomarkers for early lung cancer detection, the basic principles taught are clearly applicable to the claimed invention. Tockman et al teaches that prior to the successful application of newly described markers, research must validate the markers against acknowledged disease end points, establish quantitative criteria for marker presence/absence and confirm marker predictive value in prospective population trials (see abstract). Early stage markers of carcinogenesis have clear biological plausibility as markers of preclinical cancer and if validated (emphasis added) can be used for population screening (p. 2713s, col 1). The reference further teaches that once selected, the sensitivity and specificity of the biomarker must be validated to a known (histology/cytology-confirmed) cancer outcome. The essential element of the validation of an early detection marker is the ability to test the marker on clinical material obtained from subjects monitored in advance of clinical cancer and link those marker results with subsequent histological confirmation of disease. This irrefutable link between antecedent marker and subsequent acknowledged disease is the essence of a valid intermediate end point marker (p. 2714, see Biomarker Validation against

Acknowledged Disease End Points). Clearly, prior to the successful application of newly described markers, markers must be validated against acknowledged disease end points and the marker predictive value must be confirmed in prospective population trials (p. 2716s, col 2). In order to be useful several criteria should be taken into account including the association of SMARCD3 with the pathway to prostate cancer, modification of SMARCD3 from normal in patients at high risk for prostate cancer, shift of SMARCD3 towards normal by intervention and finally, SMARCD3 must be predictive of alteration in prostate cancer risk. As drawn to SMARCD3 being predictive of development or progression of prostate cancer risk, it is not known at what stage of carcinogenesis or recurrent carcinogenesis alteration of SMARCD3, if any, are initiated or whether those alterations are mirrored in prostate cells. The specification does not present either guidance or exemplification that would enable one of skill in the art to determine the amount of increase that would be indicative of increased risk of development or progression of prostate cancer.

In view of the above, it would be undue experimentation for one of skill in the art to practice the claimed invention.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within



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TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MINH-TAM DAVIS whose telephone number is 571-272-0830. The examiner can normally be reached on 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, JEFFREY SIEW can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SUSAN UNGAR, PH.D.  
PRIMARY EXAMINER  
